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MIESCHER'S ELASTOMA.

(Elastoma Intrapapillare Perforans Verruciforme).

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The name "elastoma intrapapillare perforans verruciforme" was first used by Miescher in 1955 to describe an unusual condition of the skin of the neck.

A study of the literature suggests that Fischer (1927) was the first to describe the disease in a patient with a circinate papular eruption on the neck. Histological examination revealed horny plugs perforating through the epidermis into the cutis and consisting of a central blue-staining amorphous mass, surrounded by a red-staining horny mantle. The central mass contained nuclear debris, inflammatory cells and conspicuous thread-like structures, the nature of which was uncertain. Within the cutis there was an inflammatory reaction of round cells and giant cells. The case was shown as an example of Kyrle's disease.

Lutz (1953) showed a case to the Swiss Association of Dermatology and Venereology under the name of keratosis follicularis serpiginosa. This was in a man of 21 who had developed the condition on both sides of the neck when he was thirteen. He had a large patch on the left and several smaller ones on the right side of the neck. Each patch consisted of atrophic areas with a few remaining follicles, surrounded by a serpiginous ridge composed of closely set keratotic nodules. At first glance, the condition looked like porokeratosis of Mibelli. Histological examination showed horny cysts beneath an unaltered epidermis.

Beening and Ruiter (1955) reported the case of a girl of 13 suffering from mongolism with a similar dermatosis of some years' duration. This consisted of depigmented circular and semicircular patches on the nape and sides of the neck, surrounded by hard, reddish nodules topped by keratotic plugs, which on removal left small dimples. The lesions cleared up slowly leaving a

serpiginous patch of papules. Histologically there was marked acanthosis and follicular hyperkeratosis with numerous superficial and deep horny cysts. Some of these were invaded by inflammatory cells, while others had disintegrated, leaving horny lamellae lying free within the cutis which showed an infiltrate of round cells, histiocytes and giant cells. The authors considered the cysts to be of sweat-duct origin and the condition identical with Lutz's hyperkeratosis follicularis serpiginosa.

In 1955, Miescher described a case in a boy of 10 with similar clinical features. His parents were healthy and there was no consanguinity. The condition had been present for a year, starting on the right side of the neck, later spreading to the nape. There were some discrete and grouped lesions, vaguely arranged in a circinate pattern on the nape of the neck and each lesion was outlined by a hyperkeratotic ridge with some inflammation at the base. This ridge consisted of closely set keratotic papules. The keratotic mass was adherent and left a bleeding crater when forcibly removed. The impression was that the ridges spread peripherally to produce irregular rings and semicircular figures, leaving central areas of slightly livid skin without atrophy. Most of the hairs within the patches were destroyed. There was no itching or pain in the affected area. The patient had a moderate degree of hyperhidrosis, mild ichthyosis on the body and lichen pilaris on the forearms. While under observation for five months, the lesions underwent involution but new patches developed.

The epidermis showed acanthosis, hyperkeratosis and hypertrophy of the rete pegs and the papillary body. In several places there were either isolated or closely set follicle-like pockets, some of which were corkscrew-like or S-shaped. They communicated at their lower ends with the underlying corium, whilst at the top they were surrounded by hyperkeratotic and parakeratotic masses. The pockets were filled with necrobiotic tissue which consisted of structureless granular debris, which stained weakly with haematoxylin and contained fragments of nuclei. There was also an admixture of parakeratotic lamellae in the upper part of the necrobiotic mass, whilst the middle and lower parts contained well preserved cells and fibres. Some looked like epidermal cells, attaining in places the appearance of "*corps ronds*". Some were histiocytes, others were giant cells, which were also present within the adjacent layer of the corium. Lymphocytes and polymorphonuclear leucocytes were scarce. The most important constituents were elastic fibres. The deeper part contained well-staining, sharply contoured, elastica which merged with the adjacent elastic network of the cutis. Above, the elastica slowly underwent degeneration, losing its staining properties and its sharp contours in the middle of the pocket. It disintegrated completely into an amorphous mass in the upper part and merged with the debris and fragmented nuclei. The middle and lower cutis were normal and the neighbouring papillae and follicles intact.

Some papillae, however, were seen to be stuffed with a dense network of elastic fibres. They were surrounded by rete pegs growing down and in, as if to envelop the " intra-epidermal elastoma ". Some of these elastomas seemed to be intra-epidermal. Because of this, Miescher came to the conclusion that the primary lesion was an intrapapillary elastoma which, owing to bad nutrition, underwent necrobiosis and was expelled on to the surface with reactive acanthosis and hyperkeratosis. He named the condition elastoma intrapapillare perforans verruciforme. As this name is rather unwieldy, I will use the eponym Miescher's elastoma. This gives credit to Miescher and stresses the importance of the elastic tissue in this condition.

Unaware of Lutz's and Miescher's cases, Grueneberg (1956) described three patients with the same condition under the name keratosis follicularis et parafollicularis serpiginosa.

More papers and presentations of cases followed in the next two years, viz., Miescher (1956*a* and *b*), Haber (1956), Marshall and Lurie (1956 and 1957), Sonck (1957), Meara (1957), D. S. Wilkinson (1958), Zambal (1958), Dammert and Putkonen (1958), Götz *et al.* (1958).

Table I gives a brief summary of all recorded cases and eight further cases not yet published.

There have been 18 males and 6 females, the age of onset ranged from 6 to 19 years and the duration of the disease at the time of the first examination from $2\frac{1}{2}$ months to 16 years. Eighteen cases occurred on the neck, two cases on the neck and the extremities, one case on the neck and cheeks, and four on the extremities only.

Clinically, the lesions all conformed fairly closely to Miescher's description. They started as a conical or flat-topped greyish-yellow or pink papule, 2 to 3 mm. in diameter and height, smooth or verrucose due to a hyperkeratotic plug. When the plug was forcibly removed a bleeding crater remained. Occasionally there was a surrounding area of inflammation. These papules were discrete or irregularly arranged or formed closed or open rings or S-shaped figures. The configuration changed according to the activity of the process as old patches disappeared and fresh ones developed. On healing, the skin was left a pinkish colour. It might show depigmentation or slight atrophy. The hair follicles might be preserved or destroyed, or as Wilkinson (1956) pointed out, the skin might look like an area epilated by diathermy. The condition was usually symptomless, but might itch occasionally.

Whilst the histology described by Miescher was confirmed in all cases, there is still considerable debate as to the pathogenesis of the condition. Ruiter (1956) seems to be the only author to agree fully with Miescher's concept of the disease. Grueneberg (1956) believes that the dermatosis starts with marked hyperkeratosis and plug formation within the follicles and sweat ducts, although it may also be extra-follicular. This hyperkeratosis ultimately

TABLE I.—*Cases Reported in the Literature.*

Author.	Sex.	Age of onset.	Duration.	Localization.	Other skin lesions.	Family history.	Remarks.
1. Fischer (1927)	M.	?	?	Neck	Not mentioned	?	Shown as Kyrle's disease.
2. Lutz (1953)	,,	13	8	,,	,, ,,	?	—
3. Ruiter (1956)	F.	9	Several years	,,	,, ,,	?	Mongolian idiocy.
4. Miescher (1955)	M.	10	2	,,	Mild ichthyosis of the legs. Lichen pilaris. Hyperidrosis	Healthy family. No consanguinity	—
5. Miescher (1956)	,,	7	16	Upper and lower extremities	Lichen pilaris in gluteal region	?	Clinically resembled Morbus Kyrle.
6. Miescher (1956)	,,	19	6/12	Neck	Not mentioned	No consanguinity. Two siblings hollow-chested	—
7. Grueneberg (1956)	,,	16	7	Neck. Upper extremities	Acneiform lesions	Parents are related to each other	Lesions appeared after an acute dermatitis.
8. Grueneberg (1956)	F.	13	6	Both elbows and arms	Not mentioned	No skin diseases in family	Koebner phenomenon.
9. Grueneberg (1956)	M.	16	2½ months	Neck	,, ,,	Nothing relevant	Keloid formation.
10. Marshall and Lurie (1956)	,,	9	4 years	,,	,, ,,	—	Keloidal tendency.
11. Marshall and Lurie (1957)	,,	11	1½ years	,,	,, ,,	No skin diseases in family	Lesions appeared after impetigo.
12. Sonck (1957)	,,	10	7 years	,,	,, ,,	—	—
13. Meara (1957)	F.	41	Had not noticed the lesion	—	Ehlers-Danlos syndrome	—	—
14. Storck (1952); Miescher (1957)	,,	17	6 years	Lower arm	Alopecia	Mother has slight club foot	Low intellect.
15. Dammert and Putkonen (1958)	M.	10	6 years	Neck	Not mentioned	Nothing known of his family	—

16. Zambal (1958)	F.	12	11 years	Neck, upper and lower extremities	Maculo- and papulosquamous lesions. Keloids. Ehlers-Danlos syndrome	One brother and one sister healthy. Father Ehlers-Danlos. Oldest sister mentally deficient and Ehlers-Danlos	Ehlers-Danlos syndrome with Kyrle-like lesions.
17. Götz *et al* (1958)	,,	16	3 years	Neck	Not mentioned	No history of this disease	—
18. Wilkinson, D. S. (1958)	M.	10	1 year	,,	,, ,,	—	Mongolism.
Cases presented to the B.A.D. as "peculiar papillary eruptions of the neck" (Haber, 1956).							
19. Morgan (1956)	M.	10	8	Neck	Not mentioned	Two brothers and 1 sister not affected	"Rather simple".
20. Wilkinson, D. S. (1956)	,,	10	1	,,	,, ,,	—	—
21. Ross (1956)	,,	19	Several months	,,	,, ,,	—	—
22. Carleton (1956)	,,	14	1 year	,,	Acne vulgaris, face	No family history	—
23. Price (1956)	,,	14	1 year	,,	Not mentioned	—	—
Personal Communications.							
24. Wilson (1958)	M.	6	4 years	Neck	Not mentioned	—	—
25. Wilkinson, I. F. (1958)	,,	10	1 year	,,	,, ,,	—	—
26. Sanderson (1958)	,,	5–6 ?	Several years	Neck and cheeks	,, ,,	—	Mongol. Biopsy refused.

perforates into the underlying corium. He states the intrapapillary condensations of elastic tissues can be found at the edge of skin grafts and tuberculous granulomata and represent nothing specific. The fibres seen within the necrobiotic masses are not elastic fibres, but " keratoid degeneration products of epidermal cells ". He regards the condition as a penetrating keratosis related to, but not identical with, Kyrle's disease.

Marshall and Lurie (1956) think that the primary change is due to ingrowing lanugo hairs which rupture through the follicle walls into the corium. They also suspect sweat ducts as possible starting points of the lesion. They find it hard to believe that the intrapapillary elastoma could be the origin of the disease. In their study of a second case (Marshall and Lurie, 1957), the authors appear uncertain, and state that " study of our second case neither confirms nor denies this theory ".

Zambal (1958) believes that the keratotic papule is due to perforation of the follicle by a hair or lanugo hair. His case occurred in one of Ehlers-Danlos syndrome and he thinks that the hyperelasticity of the skin leads to bending of a follicle, changing the course of the hair within it, which is then forced to perforate through the wall into the corium. The fibres found within the follicles, identified by Miescher as elastic fibres, are regarded by Zambal as hair and fragments of hair cuticles. Any presence of true elastic fibres is a secondary manifestation.

Dammert and Putkonen (1958) believe that the primary changes take place at the tips of the rete pegs ; " the excessive elastic tissue invades the epidermis causing destruction of the involved tissue and inflammatory reaction ". The cause of the increase of the elastica is unknown.

Götz and his co-workers believe the process starts within the follicles.

I wish to add my own observations on this remarkable disease. In 1956, I presented five cases of " a peculiar papillary eruption of the neck " to the British Association of Dermatology. They form the subject of my paper.

Case Reports.

1. *Dr. D. S. Wilkinson's case.*—I am indebted to Dr. Wilkinson for this account of his case. " In November 1954, a boy of 11, who had spent the previous year in Nigeria, was sent to see me because of an eruption which had been present on his neck for about a year and which had resisted treatment with pigmentum tinctorium and tinct. iodi. His past history had been uneventful except for rheumatic fever in 1952 while he was living in Mombasa. Towards the end of 1953, the first of these recurrent lesions occurred on the right side of the back of the neck in the form of a solitary semi-circle of rather horny spots. It was seen by a doctor who did not at that time believe it to be a ringworm infection. The patient then moved to Nigeria and the second group of lesions appeared on the left side of the neck. According to the boy's parents, there had been no recent increase in size, and the boy complained of no irritation or other symptons from the eruptions. A group of spots had been painted with iodine intermittently over the last year.

He showed a curious and rather striking picture of lesions grouped for the most part in semicircular or arcuate arrangement, forming some portion of an ellipse. Scattered in and about the same area were solitary papules. They were grouped together or near to each other, converging to form a similar arcuate arrangement. It appeared not so much that one lesion extended peripherally, as that several lesions formed in the same area, grouping together and extending outwards, one part of the circle dying away and the remainder progressing. Though there was scarcely any atrophy left in the wake of this progress, a little stippling or pocking of the skin could be seen on close examination. This light scarring was of the type seen after diathermy or electrolysis removal of hairs, but did not appear to be follicular. In fact, hairs were growing within one of the affected areas. The lesions were confined to the back of the right side of the neck and extended into the hair line. One fairly young group of lesions lay within the centre of the nuchal hair whorl but for the most part they lay below it. The colour was reddish-brown and the individual spots consisted of horny or irregularly hard papules, rather too irregular for porokeratosis of Mibelli, but resembling this more closely than any other disease that came to my mind at the time.

Biopsy was performed and photographs taken. The boy went abroad again shortly afterwards, but his father wrote two months after the biopsy had taken place, that the condition appeared to have cleared up very well excepting for two small spots which remained.

When he was seen by a colleague of mine a month after his original attendance the lesions were noted to be clearing up without treatment. They had, of course, undergone a similar variation in the past. At this time no definite diagnosis was made."

2. *Dr. J. Morgan's case.*—A boy aged 10 developed several lesions on the back of the neck. There were annular or gyrate patches surrounded by closely set pink papules some of which contained keratotic plugs. Preliminary diagnosis: late naevus? lichen planus? porokeratosis of Mibelli?

3. *Dr. R. E. A. Price's case.*—A boy aged 12 showed a circinate lesion on the back of his neck for one year. On examination he showed a ring of minute nodules, 2 cm. by 1·25 cm.

4. *Dr. Alice Carleton's case.*—A boy aged 15 complained of an irritating rash on the neck for 12 months. There was an eruption on the back and both sides of the neck consisting of pinkish partly hyperkeratotic papules arranged in irregular groups and rings (Fig. 1). Some places showed atrophy. The patient also suffered from acne. His family history was irrelevant.

5. *Dr. Aitken Ross's case.*—A boy aged 19. Annular lesions on both sides of the neck present for several months, showing centrifugal progression with central healing.

All were classical clinical examples of the condition.

Histology.

Miescher drew attention to a conspicuous and unusual proliferation and thickening of elastic fibres within the papillae (Fig. 2). He regards this "intra-epidermal elastoma" as the starting point of the development of the dermatosis which is followed by necrobiosis of the elastica, provoking down-growth of the surrounding epidermis which causes the extrusion of the whole necrobiotic mass on to the surface (Fig. 3). There seems to be no general agreement on the nature of the fibres within the necrobiotic mass. There can be no doubt, however, that these peculiar threads are elastic fibres. In

all cases I could trace direct connections between fibres and the underlying elastic network of the cutis. These fibres undergo considerable morphological change due to the action of the inflammation. They become swollen, distorted and double-contoured. Clumping of the individual fibres leads to the formation of monstrous bodies in some lesions. Some fibres show cross-striations indicating cracks.

Several sections, however, show additional features which would indicate that both sweat ducts and follicles are involved in the process. Fig. 4 shows an acanthotic rete peg containing what I consider to be an intra-epidermal

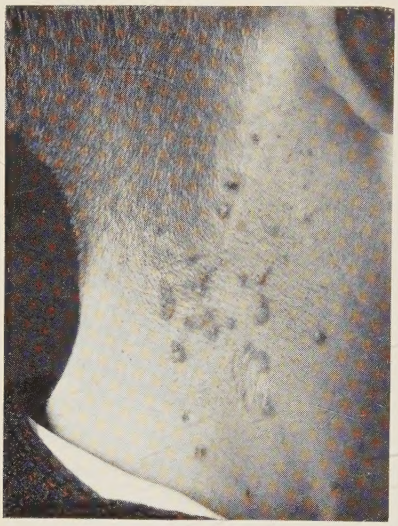

Fig. 1.

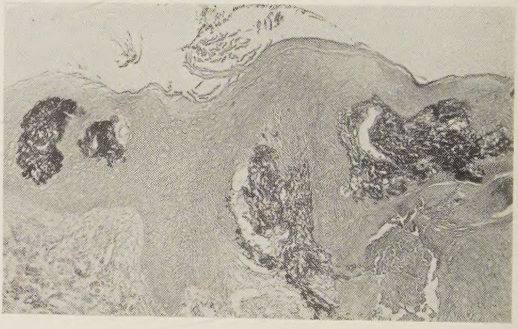

Fig. 2.

sweat duct cut in three places, containing typical necrobiotic masses, cellular debris and pycnotic nuclei. The sweat pore shows hyperkeratotic lamellae and extruded amorphous material stained dark with haematoxylin.

Fig. 5 shows necrobiotic masses extending up to the surface. On top of the upper mass there is a distinct ring of keratin, invaded by micro-organisms and undoubtedly representing a cross-section of the sweat pore (Fig. 6). Fig. 7 shows a hair follicle filled with characteristic dark-staining masses extruded through the follicular ostium. These features suggest that both follicles and sweat ducts take an active part in the pathological process. As the process shows a tendency to serpiginous spread, the intervening epidermis must also be involved.

I therefore believe that the process starts within the follicles and sweat ducts leading to a proliferation of the upper third of the appendages. Later an extension of the lesion, perhaps due to an infection, results in rupture of

either the follicular ostium or sweat duct into the underlying corium, leading to necrobiosis in a circumscribed area. The elastica shows more resistance than the collagen and therefore becomes more conspicuous.

The expulsion of the necrobiotic mass may occur either by total destruction of the epidermis, laying open the degenerated tissue which is then extruded

FIG. 3.

FIG. 4.

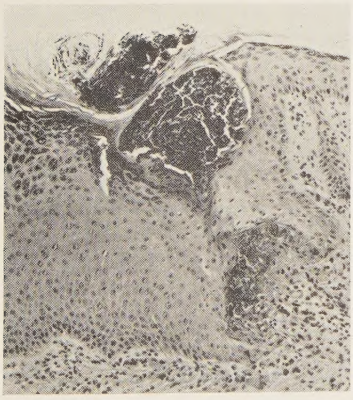

FIG. 5.

FIG. 6.

as in a papulonecrotic tuberculide, or the process comes to a halt and regeneration of the follicles or sweat ducts takes place, trapping the necrobiotic masses within their lumina and forcing them out through the ostia. This would explain the mysterious presence of elastic fibres within appendages. The tortuous arrangement of the necrobiotic tissue can also be explained in this way as it winds its way through the spiral of a sweat duct.

Miescher's contention of a primary intra-epidermal elastoma undergoing necrobiosis and perforating through the epidermis is not supported by my findings. Where the intra-epidermal elastoma is found, one encounters marked changes in the epidermis and papillary body. The surface of the epidermis looks very irregular and verrucous and the shape of the papillae varies accordingly. Perhaps this is a healed area through which the inflammatory process

Fig. 7.

has swept, leaving a distorted skin surface. The intra-epidermal elastoma may be regenerated elastica and may represent the end and not the beginning of the story.

Discussion.

The aetiology of the condition is not known. Miescher considers the intra-epidermal elastoma to be either of naevoid or infective origin, Grueneberg suspects a virus infection, Dammert and Putkonen (1958) incriminate hormonal influences and Zambal (1958) regards the condition as a " dysembryoplastic disease " in view of the fact that his case occurred in a case of Ehlers-Danlos syndrome.

It is remarkable that Meara's (1957) case of Miescher's elastoma was also associated with Ehlers-Danlos syndrome. Storck's (1952) case of Marfan's syndrome with lesions like those of Kyrle's disease on the extremities, proved histologically to be one of Miescher's elastoma (Miescher, 1957). Three cases

of mongolism showed the same condition (Ruiter, 1956; D. S. Wilkinson, 1957; Sanderson, 1958). Anning (1958) has seen a patient with Miescher's elastoma who died suddenly of a dissecting aneurism of the aorta. These cases suggest that we may be dealing with a genetically induced defect. Miescher's elastoma may be a conspicuous skin manifestation of an underlying systemic disorder.

There is no need to look for an infective aetiology in this condition; perhaps it is the soil and not the unknown agent which produces this unique histology. The fact that 18 boys and only 8 girls suffered from it suggests that non-specific trauma may be responsible for the development of the lesion. One case appeared after dermatitis (Grueneberg, 1956), one followed impetigo (Wilkinson, 1956), and one showed the Koebner phenomenon (Grueneberg, 1956).

The condition undoubtedly shows a clinical resemblance to Kyrle's disease. Miescher (1956) states that his case showed the classical clinical picture of Kyrle's disease, yet histologically revealed the typical picture of elastoma intrapapillare perforans verruciforme. He said "the question therefore remains open whether the present case is only a variant of elastoma intrapapillare perforans verruciforme which has been classified as Morbus Kyrle, or whether Morbus Kyrle itself is actually just that". A case shown by Storck (1952) as Marfan's syndrome with Kyrle's disease, proved histologically to be Miescher's elastoma (Miescher, 1957). Gruneberg also pointed out the similarity of the conditions but found them separate although perhaps related entities. Marshall and Lurie separated the conditions, but Zambal maintained that they were the same disease.

I have examined eight cases of Kyrle's disease microscopically. Apart from an entirely different histological picture, no case showed any involvement of elastic tissue.

Both conditions may perhaps simulate each other clinically, but histologically there is no evidence that the two diseases are identical or even related to each other.

Summary.

1. The clinical and histological features of Miescher's elastoma are discussed.

2. It is suggested that the process starts within the skin appendages.

3. The aetiology is unknown.

4. The condition may be a peculiar reaction to nonspecific cutaneous trauma in individuals with a genetically induced systemic disorder.

5. Kyrle's disease and Miescher's elastoma are separate conditions.

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THE RISE IN INCIDENCE OF NICKEL SENSITIVITY.

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Little information is available on variations in the incidence of allergic diseases. A report by Calnan (1956) stating that nickel sensitivity had become the most frequently demonstrated sensitivity in London in 1953–54 accordingly aroused great interest. Fisher and Shapiro (1956) stated that in New York nickel sensitivity was exceeded only by sensitivity to paraphenylenediamine, and Lahiri (1957) wrote that nickel sensitivity was a menace to Indian industry. In the Dermatological Department of the Finsen Institute we had observed a slow rise, but had not dared to regard it as real. We have therefore studied the relation of nickel sensitivity to other well known sensitivities during the years 1936–55 and attempted comparison with the use of nickel in Denmark within the same period.

The investigation was based on the total number of patients with dermatitis in the widest sense who between 1936 and 1955 had received, for purposes of research, a routine patch-test series comprising 21 substances (Bonnevie, 1939) including a test with 5% nickel sulphate. The patch tests were applied and the results read by the same technique and by the same persons throughout. The number of patients varied somewhat but did not alter qualitatively during this period. In 38,764 routine tests, 727 individuals were found to be hypersensitive to nickel.

Relation to Positive Reactors.

Fig. 1 shows the numbers of positive reactors to one or more tests: calculated per 1000 routine patch tests plotted against time, forming a curve with an almost linear horizontal course. The curve for the numbers of positive reactions to nickel per 1000 routine patch tests rises in the main, though with a minor fall for the years 1945 and 1946 (possibly 1940–46). The curve can, however, be described as a straight line with a significant slope against the horizontal line, measured by the 0·1% limit. A rise in the incidence of nickel sensitivity in proportion to the total number of reactions must thus be regarded as certain. Bonnevie (1939) found nickel sensitivity in 5·2% of all sensitive patients in 1934–35. The corresponding figure for 1936 was 7·4% and for 1955 12·9%.

Relation to Well Known Sensitivities.

Routine tests in 1936 showed nickel sensitivity to be eighth in frequency, against third in 1955, exceeded only by sensitivity to primula and balsam of Peru. Between 1936 and 1955 it became more frequent than sensitivity to

chromates (1943), colophony (1944), formalin (1946), turpentine (1950) and mercury (1955). The incidence of chromate and formalin sensitivity remained fairly constant throughout the period, but the rise in nickel sensitivity is surpassed by that to balsam of Peru, for which there is no accounting so far. Skog and Thyresson (1953) found nickel sensitivity to be rarer than chromate and formalin sensitivities in Sweden in 1948–51 and Thyresson and Skog (1953) found it rarer than chromate and turpentine sensitivities in 1951–52.

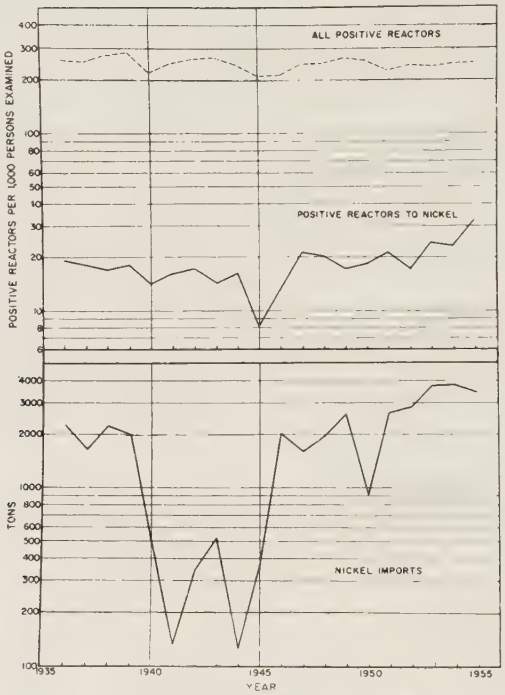

Fig. 1.

Fisher and Shapiro (1956) calculated that sensitivity to paraphenylenediamine was more frequent than that to nickel. However, sensitization to paraphenylenediamine has been almost rooted out in Denmark.

Relation to Use of Nickel in Denmark.

It is impossible to form an estimate of the amounts of nickel and nickel alloy existing in this country. As nickel is not produced here, the imports give approximate information on the amounts of nickel and nickel alloy worked up into articles for everyday use and marketed as such. The imports of ready-made articles containing nickel, on the other hand, are indeterminable.

Fig. 1 illustrates the imports of nickel and nickel alloy during the years 1936–55 compared with the number of nickel-sensitive cases per 1000 tests.

The curves show striking parallelism both in the fall during World War 2 and in the abrupt rise of the latter part of the curve. As regards the imports of nickel, these variations are plain to see in the logarithmic curve in Fig. 1. To show the significance of the variations in nickel sensitivity, regression lines have been plotted for the absolute values stated in Fig. 2 showing significant deviations from the horizontal line in relation to the 0·1 % limit. The changes in the middle curve of Fig. 1 occurred, as might be expected, somewhat later than those in the lower. However, owing to the considerable sources of error we can say no more than that a relationship is probable.

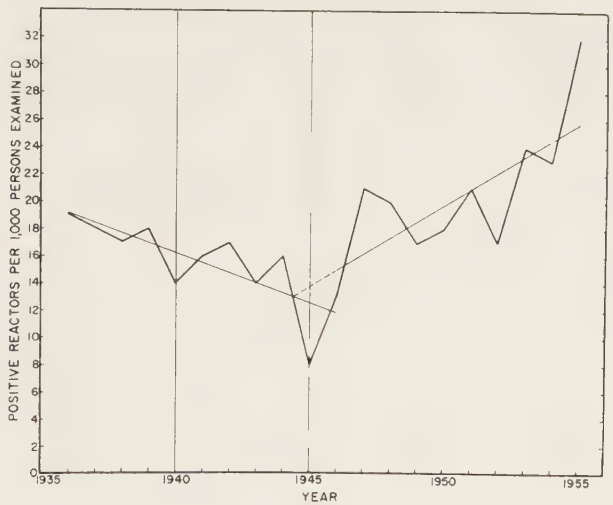

Fig. 2.

The investigations seem to show that the incidence of nickel sensitivity is rising and that this is due to increased use of metallic nickel. Sensitivity to salts of nickel seems to play no important part. Of the 727 sensitive patients only 24 were electroplaters. The direct cause of sensitization probably varies according to the character of the country. Calnan (1956) and Wells (1956) incriminate sensitization by suspenders, whereas Fisher and Shapiro (1956) take ear clips to be the most frequent cause. Lahiri (1957) has chiefly seen industrial cases. Skog and Thyresson (1953) have pointed out the rôle of a number of articles in everyday use.

To gain a general idea of the conditions in Denmark we grouped the patients with verified nickel dermatitis according to sex and occupational contact with nickel (Fig. 3). A rise is seen to have taken place independent of sex and occupation.

Further, we divided the patients according to the site where dermatitis was first observed (Table I) and compared the periods 1936–45 and 1946–55. The

TABLE I.—*Relative Regional Incidence of Nickel Dermatitis.*

Primary site of dermatitis.	Number of patients. 1936–45.	1946–55.	Rise from 1936–45 to 1946–55.
Suspender areas	150 (66·7%)	259 (65·4%)	109 (70·6%)
Hands	34 (15·1%)	80 (20·2%)	46 (135·3%)
Areas of contact with jewellery, spectacle frames, watches etc.	41 (18·2%)	57 (14·4%)	16 (39·2%)
All areas	225	396	171 (76%)

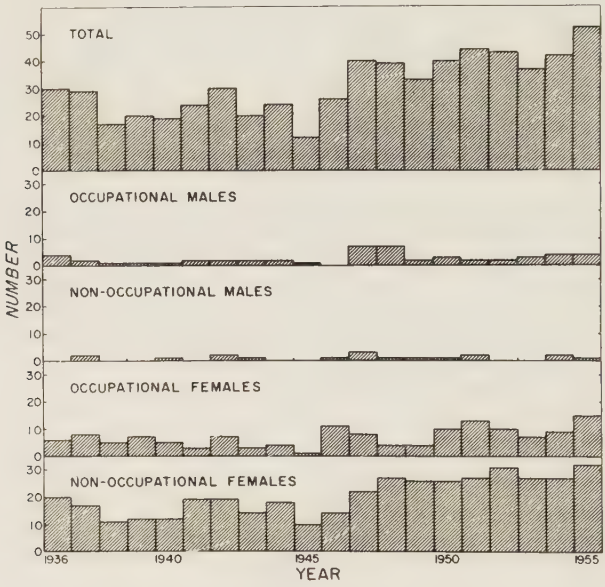

FIG. 3.

table shows that in Denmark, too, suspenders are still the chief cause, being responsible in about 65%, whereas watches, spectacle frames and jewellery play a decreasing part. A striking rise has been noticed in the small group (Bettley, 1954) of primary eczema of the hands where contact with nickel articles has been the verified cause and this will be investigated further.

SUMMARY.

During the period 1936–55 the incidence of nickel sensitivity rose appreciably in proportion to that of other known sensitivities. The curve for the rise shows close parallelism with that for nickel imports within the same period. The rise is presumably chiefly due to contact with metallic nickel and seems to be independent of sex and occupation. Suspenders are still the main cause, but the incidence of eczema of the hands brought about by nickel-containing articles in everyday use, machines and tools has shown a considerable rise. In 1955 nickel sensitivity constituted 12·9% of all verified sensitivities.

The figures for imports of nickel are published with the permission of the Danish Council of Industry.

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THE EFFECTS OF PROGESTERONE AND TESTOSTERONE ON SURFACE SEBUM AND ACNE VULGARIS.

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It has been shown that stilboestrol decreases the activity of human sebaceous glands and that consequently patients with acne vulgaris are improved (Jarrett, 1955).

Progesterone has been used in the treatment of this condition and some authors have described good results (Belisario, 1951 ; Newman and Feldman, 1954). Experimental evidence of the effect of this hormone on the sebaceous glands of rats has given conflicting results (Ebling, 1948 ; Haskin *et al.*, 1953). In view of this, it was thought worth while to investigate the effects of progesterone on human sebaceous glands by the methods employed in the stilboestrol series. The experimental findings have been correlated with the clinical state of acne patients.

Haskin *et al.* (1953) stated that progesterone had almost the same stimulating activity as testosterone on rats' sebaceous glands. The results obtained in the present progesterone series have therefore been compared with two male cases treated with the same dose of testosterone. This paper deals with the results obtained with these two hormones and discusses the pathogenesis of acne in the light of these findings.

The Value of Progesterone and Testosterone in the Treatment of Acne.

Progesterone.

This hormone has been used to a limited extent for the treatment of acne but the clinical results are not so conclusive as those with oestrogens. Way and Andrews (1950) attempted to evaluate the use of this hormone in acne, but other hormones were used in the same cases and their results are difficult to interpret. Lewis *et al.* (1951) used progesterone in doses of 6·6 mg. weekly. They considered the results unsatisfactory. On the other hand, Belisario (1951) treated thirty cases of acne with parenteral progesterone in a dose of 5 mg. weekly. He reported good results in 67% after an average period of $3\frac{1}{2}$ months' treatment. More recently Newman and Feldman (1954) have employed progesterone in cases of adult premenstrual acne. They treated ninety-five patients with parenteral progesterone, 10 mg. daily, for 10 days before an expected period. The majority of their patients was said to have

benefited from this therapy. It is of interest that these workers considered that a deficiency of the corpus luteum hormone was responsible for the premenstrual exacerbations. This view is directly opposed to that of Haskin and his collaborators who regarded progesterone as the cause of these premenstrual fluctuations (Haskin *et al.*, 1953).

Testosterone.

Van Studdiford (1935) observed the effect of a testicular extract on 27 cases of female acne. Of 9 patients given the extract alone, 7 improved. Cornbleet and Barnes (1939) treated 46 patients with 10 mg. of testosterone weekly for a period of three months or more ; 24 improved and 9 cleared completely. Riley (1939) used injections of testosterone in 20 patients ; 12 were females and 8 males. They were given up to 50 mg. weekly. The author was not favourably impressed with the therapeutic response. Molitch (1938) could find no evidence for the value of this hormone in acne. Other writers have reported the development of acne lesions in patients receiving this hormone. Thus Milco (1939) reported the appearance of acne in a male patient as a result of testosterone therapy. Hamilton (1941) treated thirty-one boys for cryptorchidism with testosterone ; most of them developed acne as a result. Although a few investigators have reported some clinical response to testosterone, most are of the opinion that androgenic hormones aggravate acne (Sulzberger and Baer, 1950). This is also supported by animal experiments which show that these hormones have a stimulating effect on sebaceous glands (Ebling, 1948). It would therefore seem likely that testosterone, when given in adequate doses, would precipitate acne, or if it were already present would cause an exacerbation.

The Effects of Sex Hormones on the Sebaceous Glands.

The effects of oestrogens on the sebaceous glands have already been reviewed (Jarrett, 1955). Ebling (1948) reported that progesterone was without effect on the sebaceous glands of rats. Later Haskin *et al.* (1953) found 360% increase in volume of the sebaceous glands in ovariectomized rats following progesterone treatment. It is possible that the discrepancy between these two findings is due to the fact that Ebling used intact animals whereas those of Haskin and his co-workers were spayed.

More recently, Lasher *et al.* (1954) failed to demonstrate an increase of the sebaceous glands after progesterone in rats whose pituitaries, ovaries and adrenals had been removed. Subsequent work by Lasher *et al.* (1955) confirmed that hypophysectomy prevented the increase in sebaceous-gland volume following progesterone treatment. The giving of pituitary gonadotropin in addition to progesterone or testosterone produced the same increase

in sebaceous volume as that obtained in ovariectomized animals. This work indicates that the pituitary is essential for the increased activity of the sebaceous glands observed in ovariectomized animals after the exhibition of progesterone or testosterone. No experiments on intact animals were reported in this series and therefore their results are not comparable with those of Ebling (1948). It is possible that progesterone increases sebaceous-gland size only in ovariectomized animals because intact animals (Ebling, 1948) and those with the ovaries and pituitary removed (Lasher *et al.*, 1955), did not show this increase.

In view of the uncertainty of the role played by progesterone in the development of acne, it was thought that it would be of value to investigate its effects on patients suffering from this condition. If the views of Haskin and his coworkers are correct, the exhibition of large doses of progesterone to acne patients should cause marked deterioration. There should also be evidence of increased activity of the sebaceous glands. The method employed in the present series to estimate the degree of activity of the sebaceous glands was the same as that previously reported in a series of patients treated with stilboestrol (Jarrett, 1955). All workers are agreed that testosterone causes a significant increase in the size and activity of sebaceous glands. Two patients were treated with the same dose of testosterone in order that the effects of these two hormones could be strictly compared.

Progesterone Series.

Six cases were included in this series of which 2 were males and 4 females. All suffered from acne of varied degrees of severity. A brief history of each case and the effects of progesterone treatment are recorded. In 3 cases, sebum readings were continued during the time they were given stilboestrol following the termination of progesterone therapy. The results are shown graphically in Figs. 1–6.

Samples were taken from three constant sites on three areas, the forehead, the nasolabial area and the back. These sites were sampled in the manner previously described in the oestrogen series and the quantity of sebum was estimated by measuring the spread on a monomolecular oil film (Jarrett, 1955). The results are expressed as regression coefficients and these have been subjected to statistical analysis.

All the patients were admitted to hospital during the period of investigation and were given progesterone in a dose of 25 mg. daily by intramuscular injection. The longest duration of treatment was 17 days and the shortest 10 days. During treatment only one patient became temporarily worse: the others remained unchanged. As none improved as a result of progesterone, they were all given a course of oral stilboestrol in order to control the activity of their lesions.

Case 1*p*.—Girl aged 18.—Mild acne of face and back of 4 years' duration. Menstrual periods were always irregular ; exacerbations of acne during menstruation. Sebum readings were taken before and during treatment. Progesterone was given for 11 days in a dose of 25 mg. daily. During this time no change was observed in the severity of her acne and there were no side-effects. Stilboestrol, 3 mg. daily, was given with good effect after stopping progesterone. The readings showed a decrease of surface sebum on the back and nasolabial areas, and an increase on the forehead during progesterone treatment. During stilboestrol therapy the sebum readings fell in all areas and her acne improved (Fig. 1).

Regression coefficients during treatment with progesterone.—Forehead : 0·2249. Nasolabial area : —1·3292. Back : —0·4049.

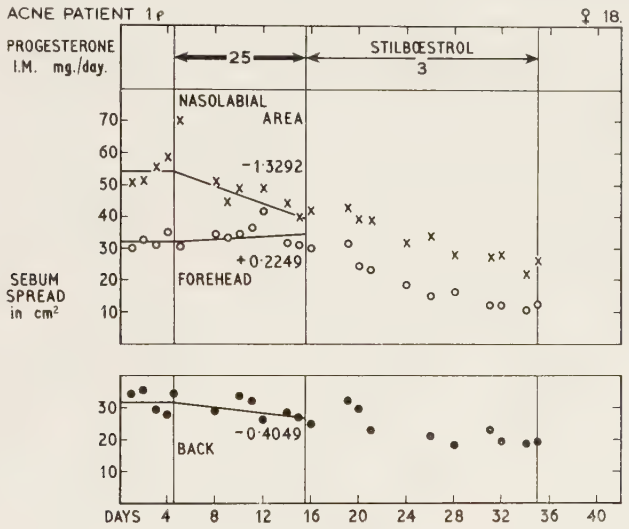

Fig. 1.

Case 2*p*.—Boy aged 18. Severe acne of face and back of 4 years' duration. Sebum readings were taken before and during treatment. Progesterone was given for 10 days and no alteration in the severity of the lesions was noted. There were no side-effects. Stilboestrol was then given as an out-patient and his acne improved. There was no marked change in his surface sebum values during treatment (Fig. 2).

Regression coefficients during treatment with progesterone.—Forehead : —0·0025. Nasolabial area : —0·4445. Back : +0·2136.

Case 3*p*.—Boy aged 15. Acne of face and back. Sebum readings were taken before and during treatment. Progesterone injections were continued for 17 days. After 6 days the acne became worse, but improved whilst progesterone was still being given and at the end of 17 days was about the same as before treatment. Stilboestrol, 3 mg. daily, was given after terminating the progesterone injections. During progesterone treatment there was a transitory rise in the surface sebum in all three areas, but the readings fell while the injections continued. The final effect was a slight increase in all areas. Subsequent stilboestrol therapy caused a decrease in all tested sites and the acne improved (Fig. 3).

Regression coefficients during treatment with progesterone.—Forehead : 0·2099. Nasolabial area : +0·3794. Back : +0·0220.

Case 4*p*.—Girl aged 18. Moderately severe acne of face and back with premenstrual exacerbations, 4 years' duration. Sebum readings were taken before and

during treatment. Progesterone was given for 14 days with no change in the severity of the acne. There were no side-effects. On stopping progesterone injections, 5 mg. of stilboestrol was given daily as an out-patient. This resulted in some improvement. Progesterone caused a small rise in the sebum in all three tested sites (Fig. 4).

Regression coefficients during treatment with progesterone.—Forehead : +1·6108. Nasolabial area : +0·6134. Back : +0·0109.

Case 5p.—Girl aged 18. Mild acne of face and back of 4 years' duration, with marked premenstrual exacerbations. Sebum readings were taken before and during treatment. Progesterone injections were given for 10 days ; during this time there

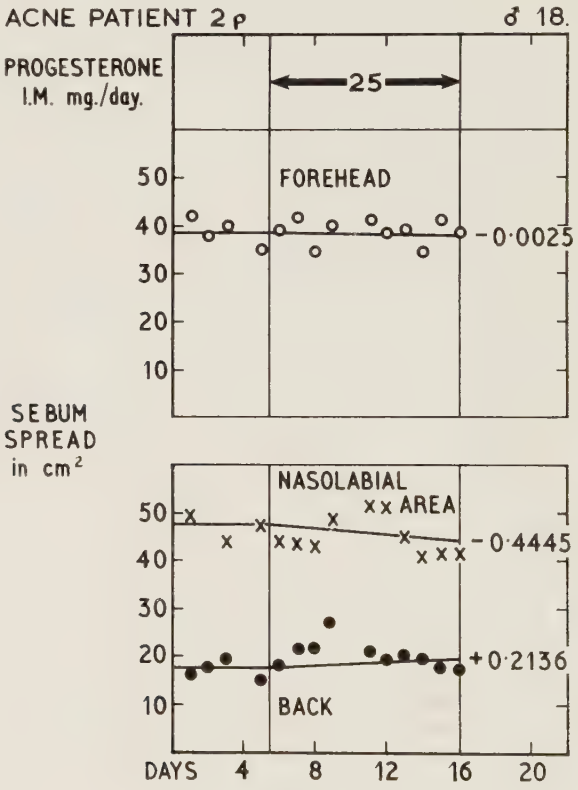

Fig. 2.

was no change in her clinical state and there were no side-effects. The surface sebum of the forehead and back were slightly increased and there was a slight decrease on the nasolabial area (Fig. 5).

Regression coefficients during treatment with progesterone.—Forehead : +0·2812. Nasolabial area : —0·6874. Back : +0·0533.

Case 6p. –Girl aged 19. Acne of moderate severity involving the face and back for 5 years, with some premenstrual exacerbations. Sebum readings were taken before and during treatment. Progesterone injections were continued for 13 days : there was neither change in the severity of her acne nor any side-effects. Stilboestrol, 3 mg. daily, was given after the cessation of the progesterone injections and this resulted in a marked improvement of the acne. Sebum readings were continued during the time she was treated with the oestrogen. During progesterone therapy

there was an increase of the surface sebum on all three tested sites. A subsequent course of stilboestrol resulted in a decrease of sebum on all these areas (Fig. 6).

Regression coefficients during treatment with progesterone.—Forehead : · 0·6145. Nasolabial area : +1.3318. Back : +0·9633.

Results.

Three areas were examined in each of the 6 patients and the values for the initial sebum levels before treatment ($\bar{y}_0$), and the mean rate of daily change

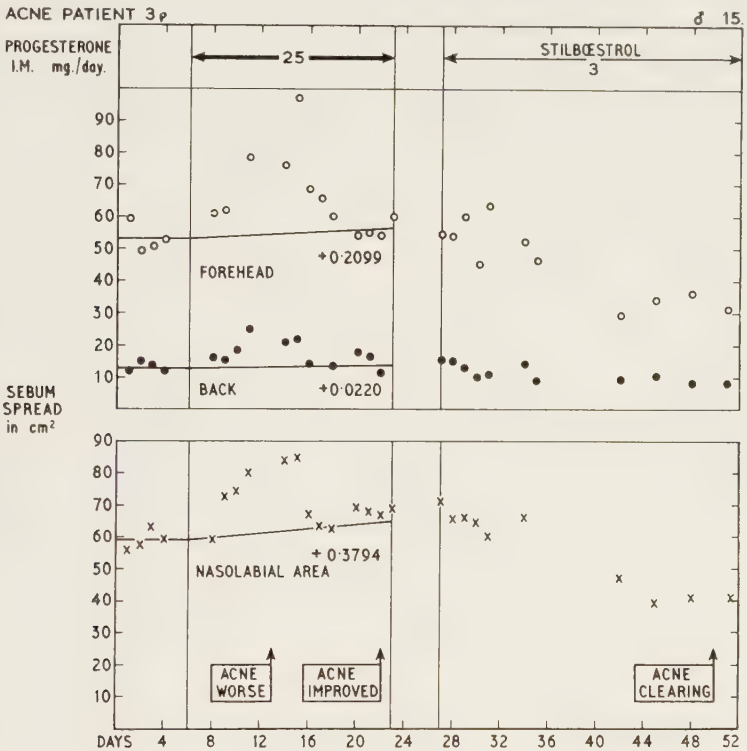

Fig. 3.

(regression coefficient, b) were calculated for all 18 areas. The mean daily change of the surface sebum was also calculated as a percentage of the initial sebum level before treatment

$$\left(\frac{100b}{\bar{y}_0}\right).$$

Of the 18 values for the regression coefficients (b), 13 were positive (an increase in surface sebum) and 5 were negative (a decrease in surface sebum). This is shown graphically in Fig. 7.

Further statistical examination showed that there was no significant difference between sebum changes occurring at different sites on the same individual.

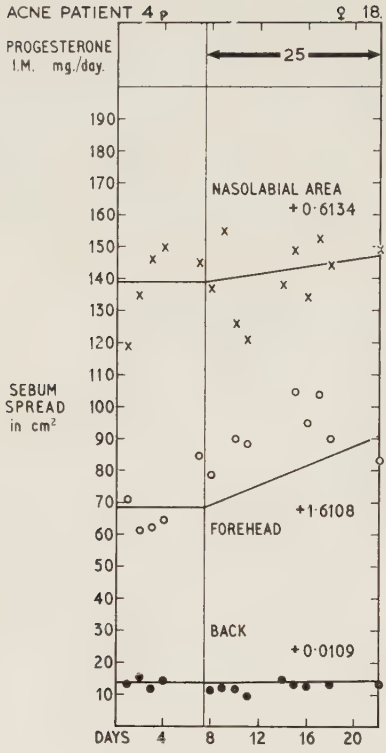

Fig. 4.

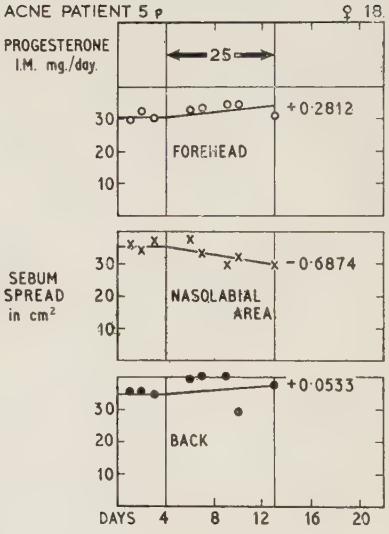

Fig. 5.

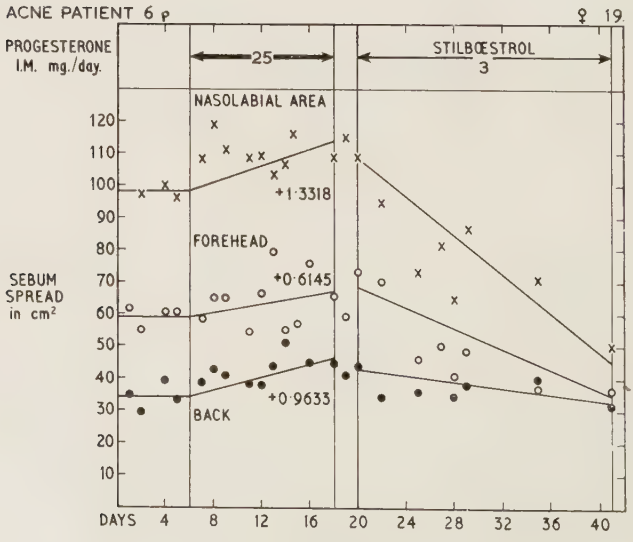

Fig. 6.

or in the changes occurring in one patient and those in another. Thus all tested sites are equally reliable as a measure of the effect of progesterone. The mean daily percentage increase in sebum spread as a result of progesterone treatment on all tested areas for all 6 patients was +0·305, and this is not significant ($t = 1·236$). Unlike the results obtained with stilboestrol (and testosterone) the effect of progesterone bears no relation to the initial sebum level before treatment and the magnitude of the mean daily change is not significantly different from zero for all tested sites. The scatter of these values around the zero line is shown in Fig. 7.

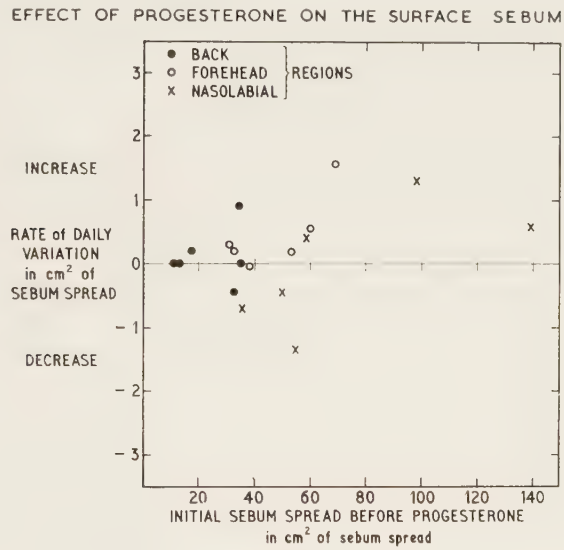

Fig. 7.

It has therefore been demonstrated that progesterone, in the dosage given, is without effect on human sebaceous glands, nor does it influence the clinical state of patients with acne vulgaris. In three cases (1*p*, 3*p*, and 6*p*), the expected decrease of surface sebum following stilboestrol therapy has been clearly shown (Figs. 1, 3, and 6). These 9 sites confirm the findings already reported in the stilboestrol series.

Testosterone Series.

Two male patients were treated with testosterone, in a dose of 25 mg. daily, by intramuscular injection. Both had mild acne involving the face and back. A brief history of each case and the surface sebum readings before and during testosterone treatment are given. In both cases the sebum readings were continued after the cessation of androgen therapy during the time they were given a subsequent course of stilboestrol. The results are expressed as in the

previous series, and they have been examined statistically. The mean rates of daily change as a percentage of the initial sebum level are shown graphically in Fig. 13.

Three areas were sampled in each case. In all six regions tested there was an increase of the surface sebum during testosterone treatment and the acne lesions became more active. Treatment was stopped, however, before the deterioration became very severe.

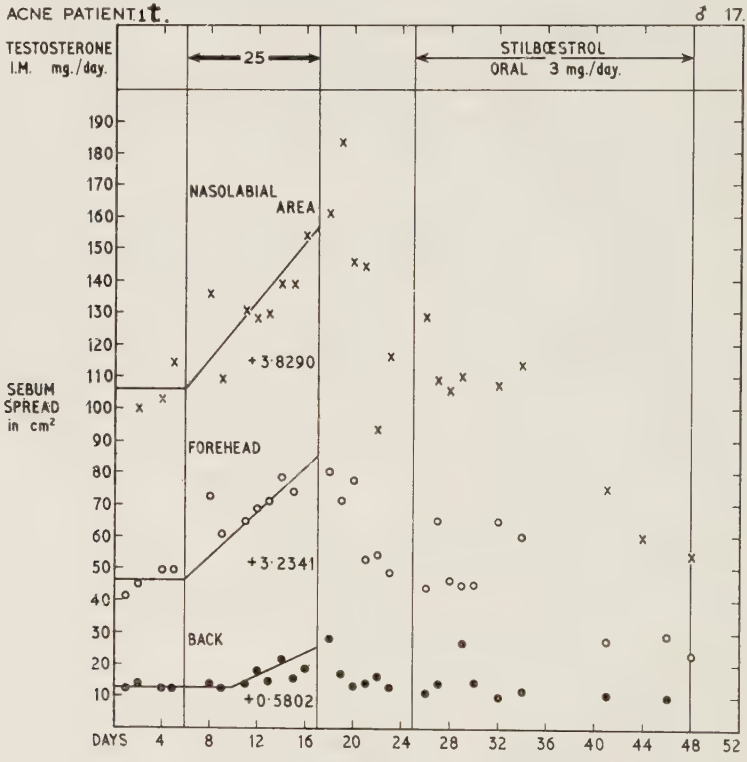

Fig. 8.

Case 1t.—Boy aged 17. Moderately severe acne of face of two years' duration. Back and chest were almost clear. The patient was given testosterone by intramuscular injection in a dose of 25 mg. daily. Surface sebum readings were taken from the face, nasolabial area and back, before and during androgen therapy. All three areas showed an increase of surface sebum (Fig. 8). After 10 days' treatment, the acne lesions became more active and the injections were stopped. During the next 10 days no treatment was given and the sebum readings decreased. Stilboestrol, 3 mg. daily by mouth, was then given and this resulted in a fall in the surface sebum readings to levels below those before the androgen was given (Fig. 8). As the sebum readings decreased there was an improvement in his clinical state. After 3 weeks' treatment with stilboestrol, the patient was given a course of ultra-violet irradiation.

Regression coefficients during treatment with testosterone.—Forehead : +3·2341. Nasolabial area : +3·8290. Back : +0·5802.

Case 2t.—Boy aged 16. Mild acne of face and chest of 3 years' duration. Surface sebum readings were taken from the forehead, nasolabial area and back, before and during therapy. The hormone was given in a dose of 25 mg. by intramuscular injection. This caused a significant increase of the surface sebum in all tested areas (Fig. 9). The injections were given for 10 days during which the lesions became more active. All treatment was stopped for 6 days and the sebum levels fell on the forehead and nasolabial region. The patient was then given stilboestrol, 3 mg. daily by mouth, for 21 days. As the patient wished to return home, surface sebum readings were recorded for only the first 13 days of this treatment (Fig. 9). Oestrogen therapy

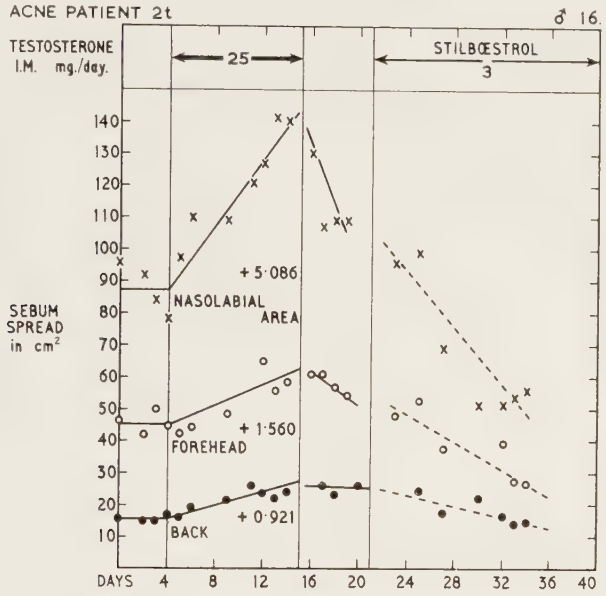

Fig. 9.

was continued as an out-patient with good effect and it was followed by a course of ultra-violet irradiation.

Regression coefficients during treatment with testosterone. Forehead : 1·560. Nasolabial area : +5·086. Back : +0·921.

Results.

As a result of testosterone treatment, a significant increase in the surface sebum of all tested areas in both patients was demonstrated. The average percentage increase of the surface sebum in the 6 areas was 5·066 and this is statistically highly significant (1% level).

When the mean daily increases (b) for all tested areas were plotted against their corresponding initial sebum levels ($\bar{y}_0$), a linear relationship was suggested (Fig. 10). Thus, the effect of testosterone is greatest in areas of high initial sebum density and least in areas of low initial sebum density. The same relationship between the mean daily change of the surface sebum and the

initial sebum levels has already been demonstrated in the stilboestrol series (Jarrett, 1955).

If, however, the increases are expressed as percentages of their respective initial sebum levels before treatment, these values are approximately the same. They are not related to the initial greasiness of the skin.

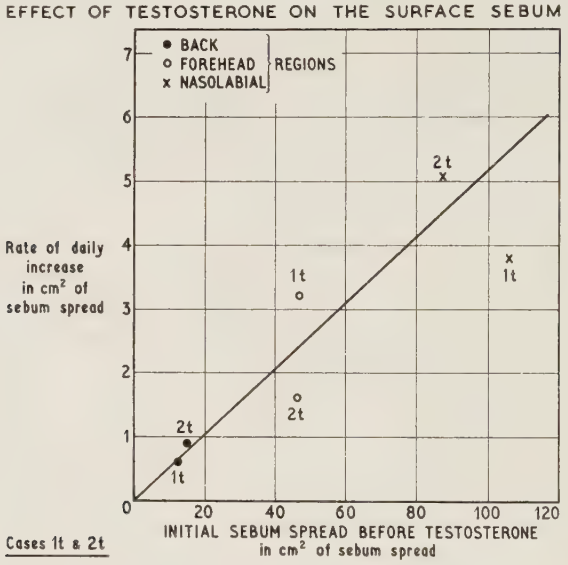

FIG. 10.

Values for the mean percentage daily increase $\left(\frac{100b}{\bar{y}_0}\right)$.—

Patient.	Forehead.	Nasolabial area.	Back.
1*t*.	6·9888	3·6169	4·5954
2*t*.	3·407	5·801	5·9884

(Average = 5·066 : significant 1% level)

This finding indicates that all areas are proportionately increased to about the same extent, which explains the clinical observation that all affected areas, whether of high or low initial sebum levels, became more active during treatment with testosterone.

Following a treatment-free period, both patients were given stilboestrol, 3 mg. daily, for 21 days and this resulted in a reduction of the surface sebum to values less than those recorded before testosterone therapy (Figs. 8 and 9). There is therefore no evidence that sebaceous glands are rendered refractory to oestrogens by a preliminary course of testosterone.

Discussion.

Progesterone Series.

It has been shown in the present series that progesterone has neither a significant effect on the surface sebum, nor any influence on the clinical state of acne patients. This lack of effect on the surface sebum confirms the findings of Ebling (1948) who found no change in the sebaceous glands of rats following the exhibition of progesterone. The conflicting results of other works (Haskin *et al.*, 1953) have already been mentioned and it is thought that these investigators obtained positive results because they treated spayed rats. Experimental evidence therefore indicates that progesterone has no effect on the sebaceous glands of intact animals and man.

Clinically, there was no indication that progesterone caused any deterioration in the condition of acne patients, nor was there any sign of improvement in the patients so treated. This fails to confirm the good results reported from the use of this hormone by Belisario (1952) and Newman and Feldman (1954).

There is also little to support the theory of Haskin and his co-workers that progesterone is related to the pathogenesis of acne in the female, or that it is responsible for the premenstrual exacerbations.

The present group of patients was given progesterone in much higher doses than have been previously used in the treatment of acne. In spite of these high doses, no detrimental effects were observed. If this hormone was related to the development of acne, one would expect to find (as with testosterone) consistent evidence of increased activity of the lesions. Only one patient (Case 3*p*) became worse, but he improved whilst the injections were still being given. It is interesting to note that during the time he became worse there was a transient rise of the surface sebum readings in all three areas which decreased as the patient improved (Fig. 3). It is most unlikely that the progesterone injections were responsible for these fluctuations.

In three patients of this series, sebum readings were taken during the period of treatment with stilboestrol. In each, the surface sebum decreased in all tested areas (Figs. 1, 3, and 6). This confirms the results previously reported in the stilboestrol series. It also shows that previous treatment with progesterone does not inhibit the action of stilboestrol: the clinical response to stilboestrol of these three patients was satisfactory.

Testosterone Series.

The effects of testosterone on the surface sebum and on the clinical state of acne patients contrasted markedly with those of progesterone. Both cases treated with testosterone showed significant increases of surface sebum in all tested areas and this was associated with exacerbation of the acne. The dose

of testosterone was the same as the dose of progesterone given in the previous series ; it is therefore difficult to support the conclusion of Haskin and his co-workers that progesterone is as powerful a stimulator of sebaceous glands as testosterone (Haskin *et al.*, 1953).

The magnitude of the mean daily increases due to testosterone has been shown to be dependent upon the initial sebum level before treatment (Fig. 10) and in this respect to resemble the mean daily decreases due to stilboestrol (Jarrett, 1955). The absolute effects of these two hormones are therefore related to the total quantity of sebaceous glandular material in the tested sites. Areas of high sebum density have numerous sebaceous glands and because of this, these hormones cause greater daily alterations of the surface sebum than in areas of low sebum density where there are fewer glands.

However, unit mass of glandular material appears to be influenced to the same extent, because when the changes as a result of treatment are expressed as percentages of their corresponding initial sebum levels, the values are approximately the same. The average value for the percentage increase in the testosterone series was +5·066 and the average percentage decrease for the stilboestrol series was −2·353 ; both these figures are statistically significant.

One would then expect that testosterone would aggravate acne lesions whether they were situated on an area of high or low surface sebum density. This is in fact what has been observed clinically ; all the tested areas became worse as a result of testosterone therapy. For the same reasons the improvement of acne lesions following stilboestrol treatment can be explained. Improvement has been demonstrated on sites of high or low initial sebum density.

Summary and Conclusions.

In a previously reported series of cases it was shown that stilboestrol decreases the activity of sebaceous glands and clinically improves cases of acne (Jarrett, 1955).

In the present series it has been shown that testosterone increases the activity of sebaceous glands and aggravates the lesions of acne vulgaris.

Progesterone, in comparable dosage to testosterone, is without effect on sebaceous glands, and does not influence the clinical state of acne patients.

The effects of these three hormones are compared in Figs. 11, 12, and 13. It will be seen that in the stilboestrol series the surface sebum is reduced on all 15 tested sites. The overall reduction is statistically significant ($t = 10{\cdot}3$). The progesterone series show a scatter around the zero line, and the effect of this hormone is not significant. The testosterone series show an increase of surface sebum in all tested areas and this increase is highly significant (1% level).

From the findings reported here there is no evidence that progesterone is

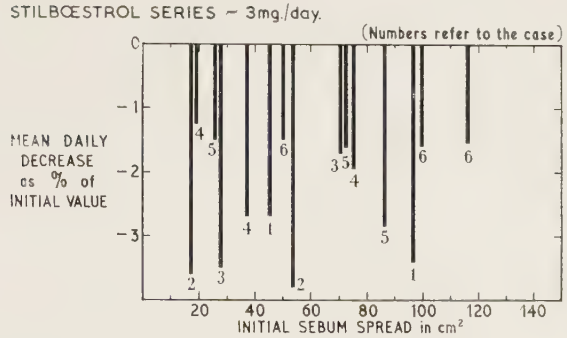

FIG. 11.

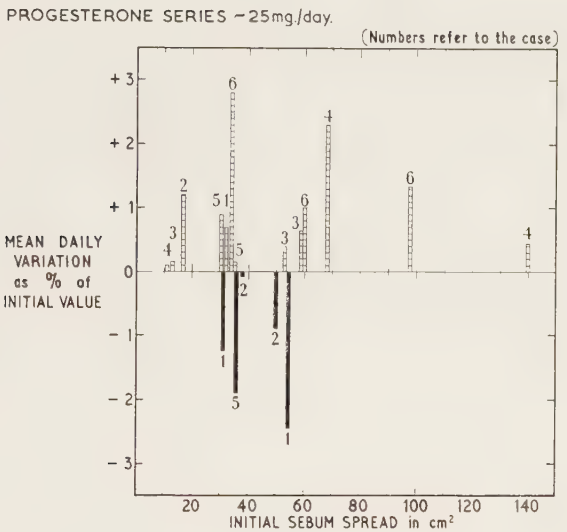

FIG. 12.

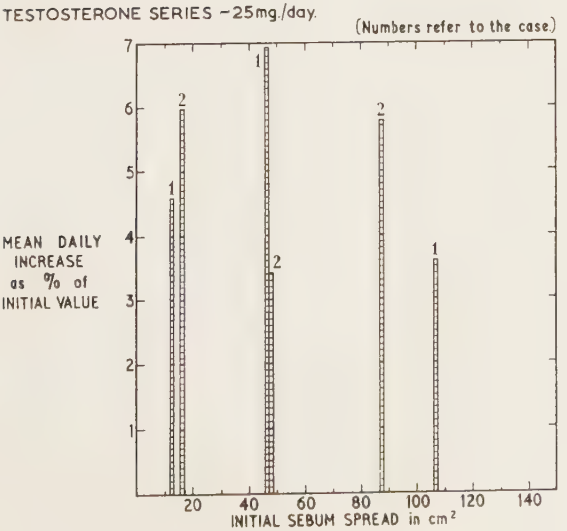

FIG. 13.

responsible for acne in female patients, that it causes the premenstrual fluctuations, or that it benefits patients suffering from acne.

I am most grateful to Dr. W. N. Goldsmith for his helpful criticism. I also thank Mr. V. K. Asta for the reproductions of the graphs and Mr. N. W. Please of University College, London, for the statistical analysis of the results.

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BOWEN'S DISEASE.

A Case Report.

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Many papers have been published on Bowen's disease after the publication of Bowen's original article (1912) on " Precancerous Dermatosis ". He described two cases where there was a solitary lesion composed of a lenticular papule which resembled nodulo-ulcerative syphiloderm. The early lesion was a firm pale red papule covered with a thickened horny layer and crust. He described one case which persisted for 19 years without any increase in the size of the lesion or any evidence of metastasis. Darier (1927) and Fraser (1928) later described a second type of Bowen's disease in which there were multiple non-elevated scaly or crusted plaques. Montgomery (1939) studied ten cases of Bowen's disease. In all but one case there were solitary plaques and all the lesions were limited to the glabrous skin. He designated those lesions as Bowen's disease which resembled Bowen's original description and the plaques described by Darier and Fraser.

Aetiology of this disease is unknown. It has sometimes been suggested to originate from the sebaceous or sweat glands but definite proofs are lacking.

All the writers on this subject agree that the condition is a form of squamous cell epithelioma *in situ* with individual cell keratinization, hyperkeratosis, acanthosis and an intact basal cell layer ; there is an infiltration with scanty lymphocytes, plasma cells and histiocytes in the upper part of the dermis. Lever (1954) considers it to be a squamous cell carcinoma *in situ* or an intra-epidermal squamous cell carcinoma rather than a precancerous dermatosis under which title it was first described by Bowen. In some cases the basal layer is broken through and a true invasive squamous cell carcinoma results.

The disease sometimes involves the mucocutaneous junction and mucous membrane specially of the vulva, vagina, cervix uteri, glans penis, prepuce and even larynx and cornea. The mucosal lesions may be intensely red, velvety and slightly thickened, indistinguishable clinically from erythroplasia ; if keratinization occurs the lesion may be mistaken for leukoplakia. Some of the skin lesions may ulcerate. The disease is practically symptomless.

Case Report.

A Hindu woman 32 years old, mother of two children, in average health, attended the clinic in August 1957. She presented lesions on the soles, dorsum of right foot, left thigh, and forearms. Some were solid elevations with firmly adherent crusts which when removed revealed a dull red oozing surface. The lesions on the soles were ulcerated with sharp and clear-cut margins resembling tertiary syphilis (Fig. 1). A serous discharge was present. The lesions varied from 2 mm. to 4 cm. in size and were very tender.

The lesions on the dorsum of right foot had appeared about one year previously : those on the soles appeared only three months ago as small scaly plaques which

Fig. 1.

gradually ulcerated. Pain started 2 months ago in the lesions on the soles as soon as they ulcerated and grew so severe that it disturbed sleep. No inguinal glands were palpable. There was no history of taking arsenic. Differential diagnosis of yaws, syphilis, tuberculides and psoriasis came in for consideration.

Laboratory examinations.—Blood W.R. and Kahn negative. Total W.B.C. and differential counts normal. Fungus could not be demonstrated in scales. Cultures for fungus and pathogenic bacteria were negative.

Histopathology.—Biopsy materials were taken from the lesions on the dorsum of right foot and from the sole.

Extensive hyperkeratosis, parakeratosis and acanthosis are present. The cells of the stratum Malpighii are completely disrupted, many cells are atypical with large nuclei and a few show mitosis. Intercellular bridges are present, these differentiating the condition from Paget's disease. Individual cell keratinization, which is the characteristic feature of Bowen's disease, is present in the stratum Malpighii. The

basal cell layer is intact. Clumping of the cells and formation of giant cells are not seen. In the subepidermal region there is moderate infiltration with lymphocytes, plasma cells and histiocytes.

These histopathological findings corroborate the diagnosis of Bowen's disease.

Available records do not show any incidence of Bowen's disease in India. Unusual features of this case are multiple painful lesions and involvement of the soles.

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CURRENT LITERATURE

THE INFLUENCE OF PRE-EXPOSURE TO DETERGENTS, SOAP AND ACETONE ON PRIMARY IRRITANT AND ALLERGIC REACTIONS. E. Skog. (1958) *Acta derm.-venereol, Stockholm*, **38**, 1.

Guinea-pigs, rabbits and humans were tested to sensitizing and primary irritant concentrations of 2,4-dinitrochloro-benzene (DNCB) after pre-exposure to alkyl benzene sulphonate detergents, soap and acetone. Such individuals reacted more strongly to the various DNCB concentrations than did control animals. O. L. S. S.

THE INFLUENCE OF SELENIUM DISULPHIDE ON SEBACEOUS GLAND VOLUMEE IN GUINEA-PIGS. E. Skog. (1958) *Acta derm.-venereol, Stockholm*, **38**, 15.

The volume of sebaceous glands, determined by the method of Haskin, Lasher and Rothman, was found to increase after exposure to selenium sulphide in shampoo. O. L. S. S.

THE CONJUGATION OF NICKEL, COBALT, HEXAVALENT CHROMIUM AND EOSIN WITH PROTEIN AS SHOWN BY PAPER ELECTROPHORESIS. I. A. Magnus. (1958) *Acta derm-venereol, Stockholm*, **38**, 21.

Paper electrophoresis at a variety of pH values was used to study the combination of these sensitizing agents with protein (cyanide-keratein, sulphide-keratein, insulin and calf thymus histone). Nickel and cobalt were found near pH 5·6 and above, eosin below pH 7 and hexavalent chromium not at all. It is suggested that nickel or cobalt combine with uncharged imidazole and amino groups. Eosin possibly reacts with the same radicles in the charged state. This would agree with the evidence that eosin remains in the stratum corneum whereas nickel and cobalt penetrate the Malpighian layer where the pH is more favourable for their combining with protein. This is an elegant experiment which makes excellent reading. O. L. S. S.

BONE MARROW STUDIES IN PSORIASIS. B. Lagerholm, A. Lodin and H. Gentele. (1958) *Acta derm.-venereol, Stockholm*, **38**, 42.

Ten patients with extensive psoriasis were investigated at the Karolinska Sjukhus by cytological and histological examination of the sternal marrow. The Unna-Pappenheim stain was modified for the purpose. Although the peripheral white blood count was normal in all cases (except one with slight eosinophilia) the authors found a constantly raised plasma cell marrow count, which they interpret as an alteration in the reticulohistiocytic system. O. L. S. S.

VITAMIN B_{12} IN THE TREATMENT OF CONGENITAL ICHTHYOSIFORM ERYTHRODERMA A. Lodin, H. Gentele and B. Lagerholm. (1958) *Acta derm.-venereol, Stockholm*, **38**, 51.

Five cases of congenital ichthyosiform erythroderma, which the authors regard as a variant of ichthyosis vulgaris, were treated with massive doses of vitamin B_{12} (1000 mg. per day for up to 3 weeks) combined with vitamin C (0·2–1·2 g. per day). No other treatment was given. Excellent results were obtained, but relapse commenced about a week after treatment was withheld. O. L. S. S.

FOLLOW-UP STUDY OF FATAL PENICILLIN REACTIONS. A Rosenthal. (1958) *J. Amer. med. Ass.*, **167**, 1118.

The records of 30 fatal reactions to penicillin occurring in New York City in less than 5 years are analysed. In 13 of them the indication for the use of penicillin was questionable and in 5 it was not indicated. The possibility of acquiring sensitivity by ingesting penicillin in milk or from immunologically related dermatophytes is discussed. In general, however, enquiry as to previous reactions to penicillin administered therapeutically and its avoidance where reactions have occurred, particularly in atopic individuals, should reduce the risk and is desirable also on medico-legal grounds. Nine fatal penicillin reactions have been the subject of lawsuits in New York. A. J. R.

CONTROL OF AXILLARY SWEATING AND OF BODY ODOR. F. Herrmann and M. B. Sulzberger. (1958) *J. Amer. med. Ass.*, **167**, 1115.

The major portion of excessive axillary sweating is of eccrine type. Aluminium salts, particularly where combined with wetting agents, reduce the output of eccrine sweat and possibly also of apocrine sweat. Antibiotics, soaps containing hexachlorophene or tetramethylthiuram disulphide, and the cation exchange resins control odour by interfering with bacterial growth. The published work on the mode of action of aluminium salts is discussed. A. J. R.

THE LABORATORY DIAGNOSIS, BIOLOGY, AND TREATMENT OF LATENT SYPHILIS. A. C. Curtis and D. S. Schuster. (1958) *J. Amer. med. Ass.*, **167**, 560.

There has been an increase in the proportion of latent syphilis to all syphilis and also in the incidence of biological false positive reactions. One of the specific treponemal antigen tests must therefore always be employed. Latent syphilis requires no more and no different treatment than does early syphilis. A total dosage of 4,800,000 units of procaine penicillin G is adequate for both. A. J. R.

THE TREATMENT OF PSORIASIS AND OTHER DERMATOSES WITH TRIAMCINOLONE (ARISTOCORT). W. B. Shelley, J. S. Harun and D. M. Pillsbury. (1958) *J. Amer. med. Ass.*, **167**, 959.

Triamcinolone, a new fluoroprednisolone compound, was used to treat 130 patients, 60 with psoriasis and 70 with various inflammatory dermatoses. Thirty-six patients with psoriasis showed a prompt response to an oral dose of 12–16 mg. daily, but invariably relapsed when the dose was reduced. The remaining 24 patients did not respond. A proportion of the patients with inflammatory dermatoses (chronic eczematous eruptions, contact dermatitis, seborrhoeic dermatitis) also responded favourably. There was no evidence of hypertension, oedema or hyperglycaemia but 2 patients showed reactivation of duodenal ulcers. Occasional side effects were epigastric discomfort and nausea, palpitations, leg cramps and attacks of vertigo. Two patients showed generalized flushing and hyperhidrosis and hirsutism was noted in 9. The authors conclude that triamcinolone should at present be reserved for the most acute or extensive and resistant cases of psoriasis. Its place in the treatment of other dermatoses requires further evaluation. A. J. R.

NUTRITION IN RELATION TO DERMATOLOGY. A. L. Lorincz. (1958) *J. Amer. med. Ass.*, **166**, 1862.

This critical and judicial review is in complete agreement with current dermatological opinion in Britain. The role of diet in the causation of skin disease has been greatly over-rated by the medical profession and still continues to receive support from many laymen. " Malnutrition in the form of overeating . . . is by far the most frequently encountered nutritional disturbance that causes or aggravates skin diseases ". Although no new facts are presented this paper is worth reading. A. J. R.

TINEA NIGRA PALMARIS. J. G. Smith, W. M. Sams and F. J. Roth. (1958) *J. Amer. med. Ass.*, **167**, 312.

Tinea nigra palmaris produces small, sharply defined patches of brownish discoloration, not scaly or elevated, and easily confused with junction naevus. Two cases acquired in Florida are reported. A. J. R.

ECHO-9 VIRUS EXANTHEMA. J. T. Prince, J. W. St. Geme, W. F. Scherer. (1958) *J. Amer. med. Ass.*, **167**, 691.

As many as 400,000 infections with a strain of Echo-9 virus are estimated to have occurred in the state of Minnesota in 1957. The infection was characterized by a morbilliform rash lasting from 1 to 3 days associated with fever and aseptic meningitis. Both the rash and the meningitis also occurred alone. A. J. R.

TREATMENT OF ALLERGIC RESPONSE TO PENICILLIN. F. O. Warren. (1958) *J. Amer. med. Ass.*, **167**, 708.

Ten patients with penicillin sensitivity reactions were treated with a combination of 300 mg. each of sodium salicylate and sodium *p*-aminobenzoate with 50 mg. of ascorbic acid. This dose

was given orally 4 times daily and completely relieved the allergic symptoms in 24–48 hours in 9 cases. In the tenth patient this dose was effective prophylactically. The treatment is empirical. A. J. R.

PRURITUS FROM AN UNUSUAL SOURCE—BIRD MITES. M. M. Cahn and F. R. Shechter. (1958) *J. Amer. med. Ass.*, **167**, 724.

A woman aged 35 developed a pruritic eruption of the face, arms and legs. *Ornithonyssus sylviarum* was found on the skin. Birds-nests infected with this mite were found in a window air-conditioner which effectively disseminated them over the patient's bedroom. The husband was not clinically affected. A. J. R.

AIDS IN EARLY DIAGNOSIS OF TUMOURS ON TIP OF NOSE. H. H. Haggart and D. J. A. Rebello. (1958) *J. Amer. med. Ass.*, **166**, 1010.

Small tumours of the tip of the nose are often difficult to diagnose clinically. Of 95 small lesions, 53 were basal cell epitheliomata and 16 were dermal cellular naevi. The inaccuracy of clinical diagnosis in this site may be due to the thickness of the skin which is adherent to underlying cartilages. The problems are discussed and adequate biopsy is recommended. A. J. R.

SOME RECENT ADVANCES IN NUTRITION. T. D. Spies. (1958) *J. Amer. med. Ass.*, **167**, 675.

This long review with many illustrations, some of which are in colour, should be read by all dermatologists. The author draws attention to the diagnostic problems presented by minimal deficiencies and to the vicious circle that may be created by nutritional deficiency and by chronic diseases which reduce the patient's ability or desire to eat. A. J. R.

ARTERIAL GRAFTING IN SEVERELY ISCHEMIC LEGS. B. Roberts and D. Hoffman. (1958) *J. Amer. med. Ass.*, **166**, 1316.

Approximately 30% of patients admitted for possible amputation of a leg were found suitable for arterial grafting. The literature is summarized and the results obtained in 20 personal cases are presented. These results are sufficiently encouraging, even in some patients over 70, to suggest that this procedure should be considered where suitable surgical facilities are available, in these otherwise intractable cases. A. J. R.

EVALUATION OF SIMPLE PRECIPITATION TEST FOR SYSTEMIC LUPUS ERYTHEMATOSUS. K. K. Jones and H. E. Thompson. (1958) *J. Amer. med. Ass.*, **166**, 1424.

An unusual precipitate was observed during the determination of serum cholesterol in a patient who later developed disseminated lupus erythematosus. As a result, a test was elaborated in which 0·1 ml. of serum or plasma is added to 2 ml. of a 12% solution of *p*-toluenesulphonic acid in glacial acetic acid. The precipitate is formed only in disseminated lupus erythematosus and its amount and character appear to be related to the severity of the disease. The test may be useful in differentiating lupus erythematosus from rheumatoid arthritis, dermato-myositis and certain other diseases and gives extremely few false-positive results. A. J. R.

THE MARCH OF ALLERGY. L. H. Criep. (1958) *J. Amer. med. Ass.*, **166**, 572.

The case records of 972 patients with various allergic disorders were analysed in an attempt to determine the degree of success achieved by treatment. The assessment must necessarily be subjective and the course of the individual case without treatment is variable and unpredictable, but the author succeeds in establishing the advantages to the patient of early and adequate treatment. A. J. R.

TOXICITY PROBLEMS OF COSMETICS. B. E. Conley. (1958) *J. Amer. med. Ass.*, **166**, 638.

Cosmetics employed for the purposes for which they are intended relatively rarely cause severe toxic or sensitization reactions, but the hazards may increase now that more pharmacologically active agents are often incorporated. The misuse of cosmetics, particularly their accidental ingestion, may involve greater dangers and the potential risk from active ingredients should perhaps be compulsorily indicated on the container. Cosmetics were involved in 3% of 15,000 reports of poisoning due to accidental ingestion of chemicals. A. J. R.